

## REMARKS

Claims 1-5, 7-11, 18, 20-25, and 27-29 remain in the application. Claims 1 and 18 have been amended. Claims 16, 17, 19, and 26 have been cancelled. A version with markings to show changes made follows page 8. Claims 18-29 were deemed to be allowable over the art. Reconsideration of this application, as amended, is respectfully requested.

Claim 1 has been rewritten to specify the identities for R<sub>1</sub> and R<sub>2</sub>. Support for this change can be found at page 5, lines 27-29 of the specification. Claim 18 has been amended to specify that R<sub>1</sub> and R<sub>2</sub> can independently be an unsubstituted aromatic or heteroaromatic group. Support for these changes can be found at page 4, line 24 through page 5, line 3 of the specification.

Claims 18-29 were rejected under 35 U. S. C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 18 has been amended, and claims 19 and 26 have been cancelled, to address this ground of rejection.

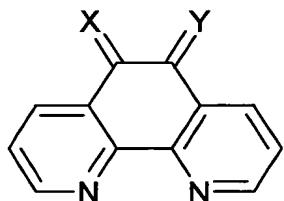
Claims 18-29 were rejected under 35 U. S. C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 has been amended, and claims 19 and 26 have been cancelled, to address this ground of rejection.

Claims 1-3 were rejected under 35 U. S. C. §103(a) as being unpatentable over Hedenmo et al. (Analyst, 1996, vol. 121, pp.1891-1895) in view of Carter et al. (USP 5,628,890). This rejection is respectfully traversed/addressed for the following reasons.

Hedenmo et al. (Analyst, 1996, vol. 121, pp.1891-1895) (hereinafter "Hedenmo et al."), discloses the mediator Os(4,4'-dimethyl,2,2'-bipyridine)<sub>2</sub>(1,10-phenanthroline-5,6-dione for the catalytic oxidation and recycling of NADH. Reagentless dehydrogenase carbon paste amperometric electrodes for glucose were developed, mixing the mediator, glucose dehydrogenase and NAD<sup>+</sup> in the paste.

Carter et al., U. S. Patent No. 5,628,890 (hereinafter "Carter et al."), discloses an electrode strip for use in an electrochemical sensor for measuring a compound in a sample, including an electrode support, a reference or counter electrode disposed on the support, a working electrode spaced from the reference or counter electrode on the support, a covering layer defining an enclosed space over the reference and working electrodes and having an aperture for receiving a sample into the enclosed space, and a plurality of mesh layers interposed in the enclosed space between the covering layer and the support, the covering layer having a sample application aperture spaced from said electrodes and said reference electrode spaced from said working electrode at a position remote from and on the opposite side of said working electrode from said aperture. The working electrode includes an enzyme capable of catalyzing a reaction involving a substrate for the enzyme or a substrate catalytically reactive with an enzyme and a mediator capable of transferring electrons transferred between the enzyme-catalyzed reaction and the working electrode to create a current representative of the activity of the enzyme and representative of the compound.

The electrode strip of claims 1-3 requires that the mediator must be:



where X and Y are independently oxygen, sulphur, CR<sup>3</sup>R<sup>4</sup>, NR<sup>3</sup>, or NR<sup>3</sup>R<sup>4</sup> or the functional group CZ<sup>1</sup>Z<sup>2</sup>, where Z<sup>1</sup> and Z<sup>2</sup> are electron withdrawing groups; and R<sup>3</sup> and R<sup>4</sup> are independently a hydrogen atom, a hydroxyl group or a substituted or unsubstituted alkyl, aryl, heteroaryl, amino, alkoxy, or aryloxy group,

Hedenmo et al. discloses a compound wherein the nitrogen atoms in the heteroaromatic rings are attached to a metal atom to form a complex. The nitrogen atoms in the heterocyclic ring of the compound of claims 1-3 are not attached to any metal atoms.

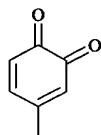
*nothing  
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Carter et al. merely discloses the use of a mediator in general. Carter et al. does not disclose or suggest the use of the compounds recited in claims 1-3 as a mediator for the reaction between nicotinamide cofactor-dependent enzyme and a nicotinamide cofactor. For the foregoing reasons, it is submitted that the combination of Hedenmo and Carter et al. does not render claims 1-3 of this application obvious to one of ordinary skill in the art.

Claims 4, 5, 7-11 were rejected under 35 U. S. C. §103(a) as being unpatentable over Hedenmo and Carter et al. in further view of Batchelor et al., "AMPEROMETRIC ASSAY FOR THE KETONE BODY 3-HYDROXYBUTYRATE", *Analytica Chimica Acta*, 221 (1989) 289-294. This rejection is respectfully traversed/addressed for the following reasons.

Batchelor et al., "AMPEROMETRIC ASSAY FOR THE KETONE BODY 3-HYDROXYBUTYRATE", *Analytica Chimica Acta*, 221 (1989) 289-294 (hereinafter "Batchelor et al."), discloses a dry-strip electrochemical sensor for the direct measurement of 3-hydroxybutyrate in blood. The sensor utilizes the electrocatalytic oxidation of enzymically generated NADH by the redox mediator 4-methyl-o-quinone. The enzyme 3-hydroxybutyrate dehydrogenase, cofactor NAD<sup>+</sup> and 4-methyl-o-quinone were incorporated into single-use disposable strip electrodes.

Batchelor refers to the use of 4-methyl-o-quinone (4-methyl-1,2-benzoquinone) as a mediator for NADH in the construction of a biosensor electrode for D-3-hydroxybutyrate, which is a ketone. The structure of 4-methyl-o-quinone is:



This mediator is no more suggestive of the mediators recited in claims 4, 5, and 7-11 of this application than are the mediators disclosed in Hedenmo et al. and Carter et al. For the foregoing reasons, it is submitted that the combination of Hedenmo, Carter et al., and Batchelor et al. does not render claims 4, 5, 7-11 of this application obvious to one of ordinary skill in the art.

Claims 16 and 17 were rejected under 35 U. S. C. § 103(a) as being unpatentable over Hedenmo and Carter et al. in further view of Hilt et al. (Chemistry, A European Journal, 1997, vol. 3(1), pp. 79-88).

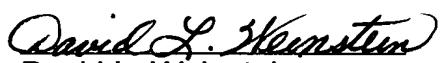
Hilt et al. (Chemistry, A European Journal, 1997, vol. 3(1), pp. 79-88)(hereinafter "Hilt et al."), discloses the synthesis as well as the electrochemical properties of homoleptic and heteroleptic (trispyridyl-methrlamine) as coligand) transition-metal complexes (Ru and Co) of 1,10-phenanthroline-5,6-dione) and of its N-monomethylated derivative.

These claims have been cancelled. Accordingly, this ground of rejection can be withdrawn.

In view of the foregoing, it is submitted that claims 1-5, 7-11, 18, 20-25, and 27-29 are in condition for allowance, and official Notice of Allowance is respectfully requested.

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Respectfully submitted,  
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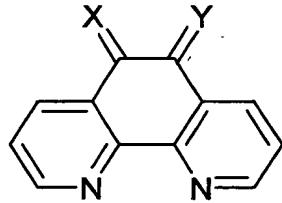
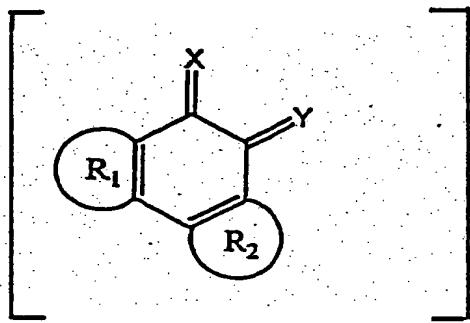
  
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Kindly rewrite claims 1 and 18 as follows:

1. (Twice amended) A single use disposable electrode strip for attachment to the signal readout circuitry of a sensor system to detect a current representative of an analyte in an aqueous sample, the strip comprising:

- a) an elongated support having a substantially flat planar surface, adapted for releasable attachment to said readout circuitry;
- b) a first conductor extending along said surface and comprising a conductive element for connection to said readout circuitry; an active electrode on said surface in contact with said first conductor, said active electrode comprising a nicotinamide co-factor-dependent enzyme, a nicotinamide cofactor, and a mediator compound having the following formula:



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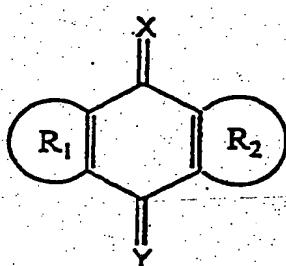
where X and Y [can] are independently [be] oxygen, sulphur, CR<sup>3</sup>R<sup>4</sup>, NR<sup>3</sup>, or NR<sup>3</sup>R<sup>4</sup> or the functional group CZ<sup>1</sup>Z<sup>2</sup>, where Z<sup>1</sup> and Z<sup>2</sup> are electron withdrawing groups; [R<sub>1</sub> is a six-membered unsubstituted or substituted heteroaromatic ring having nitrogen in the 1-position and R<sub>2</sub> is a six-membered unsubstituted or substituted heteroaromatic ring having nitrogen in the 10-position;] and R<sup>3</sup> and R<sup>4</sup> [can] are

independently [be] a hydrogen atom, a hydroxyl group or a substituted or unsubstituted alkyl, aryl, heteroaryl, amino, alkoxy, or aryloxy group, wherein said active electrode is formulated with filler and binder ingredients;

- c) a second conductor extending along said surface, comprising a conductive element for connection to said readout circuitry;
- d) a reference/counter electrode in contact with said second conductor;
- e) said conductors being spaced apart so as not to be in electrical contact and being configured so as not to be brought into electrical contact when said aqueous sample is placed on said strip;
- f) said active electrode and said reference/counter electrode being configured so that both may be simultaneously covered by a small drop of said aqueous sample to provide an electrical conduction path between said electrodes.

18. (Once amended) A single use disposable electrode strip for attachment to the signal readout circuitry of a sensor system to detect a current representative of an analyte in an aqueous sample, the strip comprising:

- a) an elongated support having a substantially flat planar surface, adapted for releasable attachment to said readout circuitry;
- b) a first conductor extending along said surface and comprising a conductive element for connection to said readout circuitry; an active electrode on said surface in contact with said first conductor, said active electrode comprising a nicotinamide co-factor-dependent enzyme, a nicotinamide cofactor, and a mediator compound having the following formula:



where X and Y [can] are independently [be] oxygen, sulphur, CR<sup>3</sup>R<sup>4</sup>, NR<sup>3</sup>, or NR<sup>3</sup>R<sup>4</sup> or the functional group CZ<sup>1</sup>Z<sup>2</sup>, where Z<sup>1</sup> and Z<sup>2</sup> are electron withdrawing groups; [R<sub>1</sub> is a six-membered unsubstituted or substituted heteroaromatic ring having nitrogen

in the 1-position and R<sub>2</sub> is a six-membered unsubstituted or substituted heteroaromatic ring having nitrogen in the 8-position] R<sub>1</sub> and R<sub>2</sub> are independently an unsubstituted aromatic or heteroaromatic group; and R<sup>3</sup> and R<sup>4</sup> [can] are independently [be] a hydrogen atom, a hydroxyl group or a substituted or unsubstituted alkyl, aryl, heteroaryl, amino, alkoxy, or aryloxy group, wherein said active electrode is formulated with filler and binder ingredients;

- c) a second conductor extending along said surface, comprising a conductive element for connection to said readout circuitry;
- d) a reference/counter electrode in contact with said second conductor;
- e) said conductors being spaced apart so as not to be in electrical contact and being configured so as not to be brought into electrical contact when said aqueous sample is placed on said strip;
- f) said active electrode and said reference/counter electrode being configured so that both may be simultaneously covered by a small drop of said aqueous sample to provide an electrical conduction path between said electrodes.